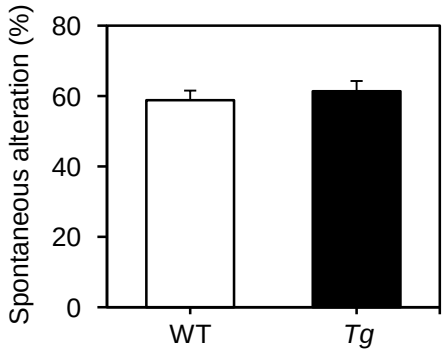
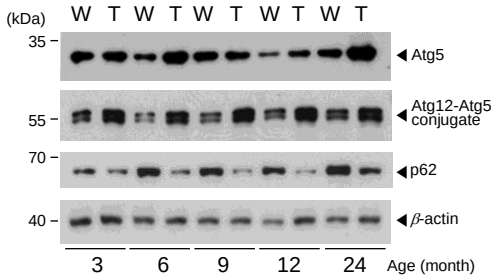
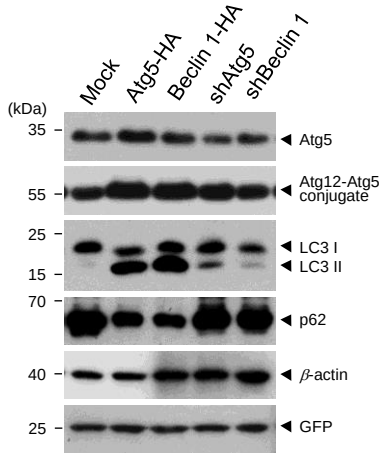


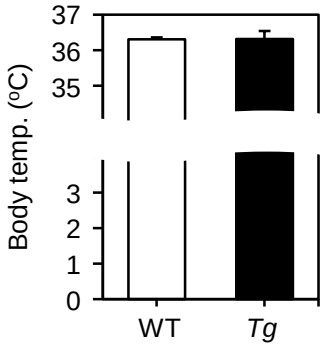
Supplementary Figure S1. Y-maze test. Memory function was examined in 14-month-old WT and Atg5 *Tg* mice (*n* = 6) using the Y-maze test. Bars represent the mean ± S.E.M.



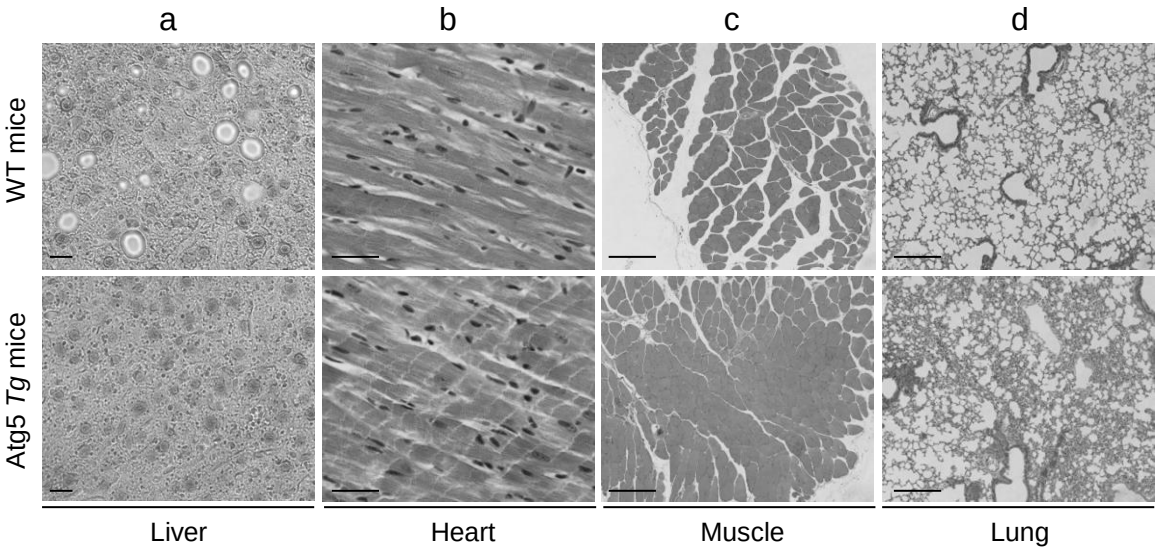
Supplementary Figure S2. Expression levels of Atg5, Atg12-Atg5 conjugate, and p62 in the indicated ages of WT and Atg5 *Tg* mice. Whole tissue extracts were prepared from the heart of Atg5 *Tg* mice and WT littermates and analyzed by western blotting using the indicated antibodies. *β*-Actin served as a control .



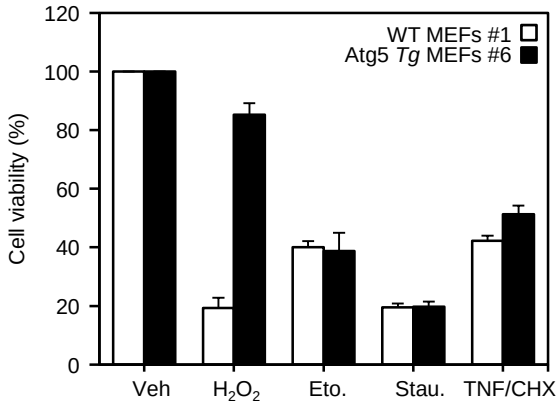
Supplementary Figure S3. Overexpression effect of Atg5 on autophagy activity in cells. HEK293T cells were transfected with pcDNA (Mock), Atg5, beclin 1, Atg5 shRNA or beclin 1 shRNA for 48 h. Whole cell lysates were prepared and subjected to immunoblotting using the indicated antibodies. *β*-Actin served as a control and GFP as an internal control.



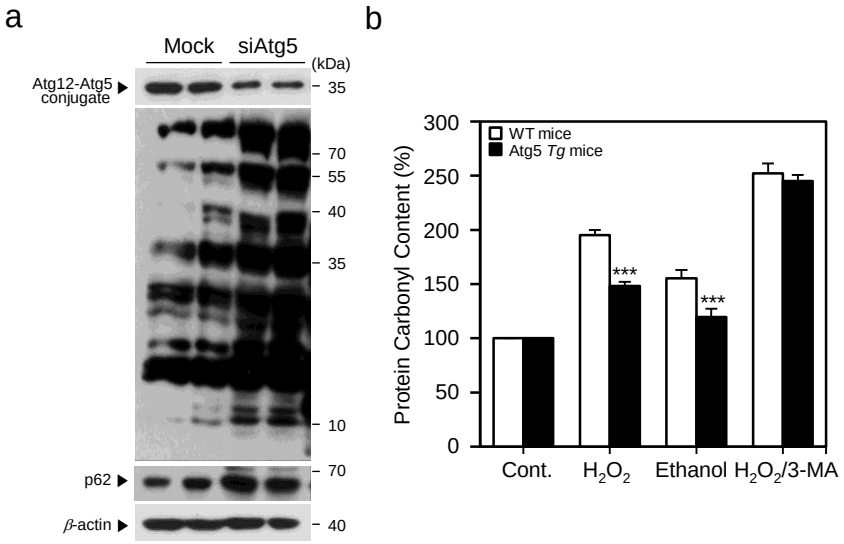
Supplementary Figure S4. Measurement of body temperature in Atg5 *Tg* mice. For measuring temperature, mice were anesthesia with pentobarbital sodium and implanted with thermometer at the indicated times (*n* = 15 for WT and Atg5 *Tg* mice, respectively). Bars represent the mean ± S.E.M.



Supplementary Figure S5. Morphology of the liver, heart, muscle, and lung in WT and Atg5 *Tg* mice. Paraffin sections of mouse tissues were stained with hematoxylin and eosin. (Scale bars - Liver, 50 μm; Heart, 25 μm; Muscle, 100 μm; Lung, 100 μm, Olympus, x100).



Supplementary Figure S6. Comparison of the relative sensitivities of WT and Atg5 *Tg* MEFs to various cell death signals. Primary cultured (passage #3) Atg5 *Tg* MEFs were treated for 24 h with H_2O_2 (300 µM), etoposide (40 µM), staurosporine (20 nM) or TNF-α (30 ng/ml)/Cycloheximide (0.5 µg/ml). Cell viability was then assessed after propidium iodide staining. Bars represent the mean ± S.E.M (*n* = 3).



Supplementary Figure S7 . Change in the level of protein oxidation by Atg5 expression. (**a**) Enhanced protein oxidation in the liver of mice following Atg5 knockdown. After tail vein injection of control (Mock) or small interfering RNA (siRNA)-Atg5 into 12-month-old WT mice for 5 days, whole liver tissue lysates were prepared and analyzed with immunoblotting using anti-Atg5 and anti-DNP antibodies. β-Actin served as a control. (**b**) Reduced protein oxidation in Atg5 *Tg* MEFs. WT and Atg5 *Tg* MEFs were left untreated or treated with ethanol (100 mM) for 1 h or H_2O_2 (1 mM) in the presence or absence of 3-MA (2.5 mM). The protein oxidation was determined using ELISA (Sigma). The values represent the mean ± S.D. of four independent measurements (*** p<0.005; Student's t-test).

	WT, *n* = 100	Atg5 *Tg*, *n* = 100
Cancer	No	No
Hepatocellular inclusions	No	No
Skin ulcerations	No	No
Skin atrophy	No	No
Hair graying	No	No
Body weight	No difference	Reduced
Plasma levels	No difference	No difference
Fertility		
Female	No difference	No difference
Male	No difference	No difference
Memory	No	No

Supplementary Table S1. Overview of Atg5 *Tg* mice phenotype. For comparison of phenotype, mice were continuously examined from neonatal stage to death (*n* = 200).

	3-month-old (*n* = 12)		24-month-old (*n* = 4)		
	WT	**Atg5 *Tg***	**WT**	**Atg5 *Tg***	Reference (Range)
WBC, K/μl	5.16 ± 1.2	7.81 ± 0.9	7.2 ± 1.4	8.5 ± 0.45	1.8 - 10.7
NE, K/μl	1.4 ± 0.9	0.91 ± 1.2	1.67 ± 0.377	1.39 ± 0.3	0.1 - 2.4
LY, %	3.20 ± 0.92	6.42 ± 1.2	5.48 ± 0.53	7.62 ± 1.13	0.9 - 9.3
MO, K/μl	0.35 ± 1.4	0.4 ± 1.0	0.37 ± 0.035	0.35 ± 0.04	0.0 - 0.4
EO, K/μl	0.17 ± 0.08	0.08 ± 0.08	0.155 ± 0.026	0.12 ± 0.025	0.0 - 0.2
RBC, M/μl	10.92 ± 0.9	10.6 ± 1.2	7.88 ± 1.17	9.12 ± 0.3	6.36 - 9.42
Hb, g/dL	14.9 ± 0.3	14.9 ± 0.9	14.05 ± 0.67	14.72 ± 0.36	11.0 - 15.1
HCT, %	41.5 ± 1.2	39.8 ± 1.3	44.59 ± 2.848	39.98 ± 1.64	35.1 - 45.4
MCV, fL	38 ± 2.1	37.5 ± 2.4	46.25 ± 3.197	41.75 ± 2.5	45.4 - 60.3
MCH, pg	13.6 ± 1.8	14.1 ± 1.2	16.79 ± 1.65	17.42 ± 2.5	14.1 - 19.3
MCHC g/dL	35.9 ± 2.2	37.4 ± 2.8	30.278 ± 1.08	34.82 ± 1.38	30.2 - 34.2
RDW, %	19.2 ± 1.3	18.6 ± 1.5	19.91 ± 1.67	19.48 ± 0.69	12.4 - 27.0
PLT, K/μl	326 ± 4.8	342 ± 5.1	433.75 ± 15.5	425.5 ± 4.8	592 - 2972
MPV, fL	5.1 ± 1.1	5.4 ± 0.9	6.98 ± 0.48	5.65 ± 0.48	5.0 - 20.0

Supplementary Table S2. Cell index in whole blood from WT and Atg5 *Tg* mice #25. For hematological test, blood was collected from 3- and 24-month-old mice (*n* = 12 for 3-month-old, *n* = 4 for 24-month-old WT and Atg5 *Tg* mice #25). Fourteen parameters of blood count were examined using Multi-species HEMAVET Hematology System. Data are displayed as mean ± S.E.M.